Regimen Monograph

A - Regimen Name

BEACOPP Regimen

Bleomycin-Etoposide-ADRIAMYCIN ® (DOXOrubicin)-Cyclophosphamide-ONCOVIN ® (VinCRIStine)-Procarbazine-Prednisone

Disease Site
Hematologic
Lymphoma - Hodgkin

Intent
Curative

Regimen Category
Evidence-Informed :

Regimen is considered appropriate as part of the standard care of patients; meaningfully improves outcomes (survival, quality of life), tolerability or costs compared to alternatives (recommended by the Disease Site Team and national consensus body e.g. pan-Canadian Oncology Drug Review, pCODR). Recommendation is based on an appropriately conducted phase III clinical trial relevant to the Canadian context OR (where phase III trials are not feasible) an appropriately sized phase II trial. Regimens where one or more drugs are not approved by Health Canada for any indication will be identified under Rationale and Use.

Rationale and Uses
Treatment of unfavourable or advanced stage Hodgkin's lymphoma, in patients who are 15-65 years of age.

Supplementary Public Funding
procarbazine
ODB - General Benefit (procarbazine)

prednisone
ODB - General Benefit (prednisone)

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B - Drug Regimen

The dosing below is for **escalated BEACOPP**:

cyclophosphamide	1250 mg /m²	IV	Day 1
DOXOrubicin	35 mg /m²	IV	Day 1
etoposide	200 mg /m²	IV	Days 1 to 3
procarbazine	100 mg /m²	PO	Daily, on days 1-7
prednisone	40 mg /m²	PO	Daily, on days 1-14
vinCRIStine	1.4 mg /m²	IV (max 2 mg)	Day 8
bleomycin	10 units /m²	IV	Day 8

filgrastim
Use as primary prophylaxis.

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C - Cycle Frequency

REPEAT EVERY 21 DAYS

For a usual total of 6 to 8 cycles unless disease progression or unacceptable toxicity occurs

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D - Premedication and Supportive Measures

Antiemetic Regimen: Moderate (D1-7)
Minimal (D8)

Febrile Neutropenia Risk: High

Other Supportive Care:

- Consider measures to preserve fertility or sperm/ovum banking.

Also refer to CCO Antiemetic Recommendations.

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E - Dose Modifications

Doses should be modified according to the protocol by which the patient is being treated.

Dosage with toxicity

On day 1 of cycle, platelets must be ≥ 100 x 10^9/L and ANC ≥ 1 x 10^9/L and toxicities recovered to ≤ grade 2.

Dose Levels:

	Dose level 1 (standard BEACOPP)	**Dose level 2**	**Dose level 3**	**Dose level 4**	**Dose level 5 (escalated BEACOPP)**
Doxorubicin	25	35	35	35	35
Cyclophosphamide	650	800	950	1100	1250
Etoposide	100	125	150	175	200

Dosage with Toxicity:

Toxicity (Counts x 10^9/L or Grade)[1]	**Action (dose level or % previous dose)**
Grade 4 AGC >4 days Grade 4 platelets Febrile neutropenia	↓ 1 dose level [2]
Grade 4 GI	↓ 1 dose level [2]
Delay > 2 weeks	↓ 2 dose levels or ↓ to standard BEACOPP (dose level 1)
Treatment delay of 1-2 weeks	↓ 1 dose level [2]
Grade 3 other toxicity	Consider ↓ 1 dose level
Grade 4 other toxicity	Discontinue or ↓ 1 to 2 dose levels
Cardiotoxicity[3]	Discontinue doxorubicin

[1]On day 1 of cycle, platelets must be ≥ 100 x 10^9/L and ANC ≥ 1 x 10^9/L and toxicities recovered to ≤ grade 2.

[2]If toxicity requiring dose decrease/delay recurs on next cycle, reduce to dose level 1. If recurs at other cycles, reduce by 2 dose levels.

[3]including any signs and symptoms of heart failure, greater than 10% decline in LVEF to below the lower limit of normal, a greater than 20% decline in LVEF from any level, or LVEF ≤ 45%.

Neurotoxicity:

Symptom	% usual dose of Vincristine
areflexia only	100 %
abnormal buttoning, writing	67 %
moderate motor neuropathy (± cranial)	Hold until recovery then reduce dose by 50%
severe motor neuropathy	Omit

Hepatic Impairment

AST/ALT	Bilirubin	Bleomycin	Etoposide	Doxorubicin	Cyclophosphamide	Vincristine	Procarbazine
		(% previous dose)					
	1-2 x ULN	No change	50%	50%	No change	50%	75%
5-10 x ULN	> 2 - 4 x ULN	No change	25%	25%	Caution	25%	OMIT
> 10 x ULN	> 4 x ULN	No change	OMIT	OMIT	Caution	OMIT	OMIT

Renal Impairment

Creatinine Clearance (mL/min)	Bleomycin	Etoposide	Doxorubicin	Cyclophosphamide	Vincristine	Procarbazine
	(% previous dose)					
>30-50	75%	No change	No change	50-75%	No change	Consider dose reduction
10-30	75%	No change	No change	50% or OMIT	No change	Consider dose reduction
<10	50%	50% or OMIT	No change	OMIT	No change	Consider dose reduction or OMIT

Dosage in the Elderly

No dose modification routinely required for cyclophosphamide, but should be used with caution. Use doxorubicin with caution. No dose adjustment required for etoposide. Older patients may have more neurotoxicity with vincristine.

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F - Adverse Effects

Refer to cyclophosphamide, DOXOrubicin, etoposide, procarbazine, prednisone, vinCRIStine, bleomycin, filgrastim drug monograph(s) for additional details of adverse effects

Most Common Side Effects	Less Common Side Effects, but may be Severe
. • Alopecia • Nausea, vomiting • Myelosuppression ± infection, bleeding (may be severe) • Diarrhea/constipation • Mucositis • ↑ LFTs • Dizziness • GI irritation (may be severe, including perforation) • Hyperglycemia • Insomnia • Muscle weakness • Phlebitis, vesicant • Neuropathy (may be severe) • Hemorrhagic cystitis • Reproductive risk	• Hypersensitivity • Hyperuricemia • Adult respiratory distress syndrome (ARDS) • Pneumonitis • Arterial thromboembolism • Venous thromboembolism • CNS effects • Glaucoma • Cardiotoxicity • Nephrotoxicity • Pancreatitis • Secondary malignancy • Radiation recall • Rash • DIC/HUS/hemolysis

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G - Interactions

Refer to cyclophosphamide, DOXOrubicin, etoposide, procarbazine, prednisone, vinCRIStine, bleomycin, filgrastim drug monograph(s) for additional details

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H - Drug Administration and Special Precautions

Refer to cyclophosphamide, DOXOrubicin, etoposide, procarbazine, prednisone, vinCRIStine, bleomycin, filgrastim drug monograph(s) for additional details

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I - Recommended Clinical Monitoring

Treating physicians may decide to monitor more or less frequently for individual patients but should always consider recommendations from the product monograph.

Recommended Clinical Monitoring

- Clinical toxicity assessment (including local toxicity, urogenital, GI, neurotoxicity, bleeding tendency, cardiotoxicity and pulmonary); at each visit
- CBC; baseline and before each cycle. Interim counts should be done in first cycle and repeated if dose modifications necessary.
- Blood glucose testing; baseline and regular.
- Regular chest x-ray and routine pulmonary function test
- Baseline and regular liver and renal function tests (including electrolytes and magnesium), and urinalysis.
- Cardiac examination especially with risk factors (including prior therapy with Epirubicin, Mitoxantrone, and other cardiotoxic drugs), or a cumulative doxorubicin dose of > 450mg/m^2.
- Baseline blood pressure at each treatment; monitor for hypotension.

- Grade toxicity using the current NCI-CTCAE (Common Terminology Criteria for Adverse Events) version

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J - Administrative Information

Prednisone, Procarbazine, Filgrastim: Outpatient prescription for home administration

Approximate Patient Visit	Day 1: 2 hours; Days 2, 3: 1 hour; Day 8: 0.5 hour
Pharmacy Workload (average time per visit)	22.114 minutes
Nursing Workload (average time per visit)	43.729 minutes

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K - References

Diehl V, Franklin J, Hasenclever D, et al. BEACOPP, a New Dose-Escalated and Accelerated Regimen, Is at Least as Effective as COPP/ABVD in Patients With Advanced-Stage Hodgkin's Lymphoma: Interim Report From a Trial of the German Hodgkin's Lymphoma Study Group. J Clin Oncol 1998;16:3810-21.

Diehl V, Franklin J, Pfreundschuh M, et al.Standard and Increased-Dose BEACOPP Chemotherapy Compared with COPP-ABVD for Advanced Hodgkin's Disease. N Engl J Med 2003;348:2386-95.

Engert A, Diehl V, Franklin J, et al. Escalated-Dose BEACOPP in the Treatment of Patients With Advanced-Stage Hodgkin's Lymphoma: 10 Years of Follow-Up of the GHSG HD9 Study. J Clin Oncol 2009;27:4548-4554.

Federico M, Luminari S, Iannitto E, et al. ABVD Compared With BEACOPP Compared With CEC for the Initial Treatment of Patients With Advanced Hodgkin's Lymphoma: Results From the HD2000 Gruppo Italiano per lo Studio dei Linfomi Trial. J Clin Oncol 2009;27:805-811.

Tesch H, Diehl V, Lathan B, et al. Moderate Dose Escalation for Advanced Stage Hodgkin's Disease Using the Bleomycin, Etoposide, Adriamycin, Cyclophosphamide, Vincristine, Procarbazine, and Prednisone Scheme and Adjuvant Radiotherapy: A Study of the German Hodgkin's Lymphoma Study Group. Blood 1998;92:4560-4567.

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M - Disclaimer

Regimen Abstracts

A Regimen Abstract is an abbreviated version of a Regimen Monograph and contains only top level information on usage, dosing, schedule, cycle length and special notes (if available). It is intended for healthcare providers and is to be used for informational purposes only. It is not intended to constitute or be a substitute for medical advice, and all uses of the Regimen Abstract are subject to clinical judgment. Such information is provided on an "as-is" basis, without any representation, warranty, or condition, whether express, or implied, statutory or otherwise, as to the information's quality, accuracy, currency, completeness, or reliability, and Cancer Care Ontario disclaims all liability for the use of this information, and for any claims, actions, demands or suits that arise from such use.

Information in regimen abstracts is accurate to the extent of the ST-QBP regimen master listings, and has not undergone the full review process of a regimen monograph. Full regimen monographs will be published for each ST-QBP regimen as they are developed.

Regimen Monographs

Refer to the New Drug Funding Program or Ontario Public Drug Programs websites for the most up-to-date public funding information.

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